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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/284,320	06/21/99	KATO	S GIN-6705CPUS

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EXAMINER	
SEHARASEYON,J	
ART UNIT	**PAPER NUMBER**
1647	22

DATE MAILED: 08/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev. 2/95)
*U.S. GPO: 2000-473-000/44602

FILE COPY.

Office Action Summary	Application No. 09/284,320	Applicant(s) KATO ET AL.	
	Examiner Jegatheesan Seharaseyon	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *11 June 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

-DETAILED ACTION

1. This office action is in response to the amendment and response filed on 6/11/01 in Paper No: 21. Claims 2-5 have been cancelled and claims 6-18 have been added. Therefore, claims 6-18 are pending.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

3. Applicants' figures have been approved by the draftsman.

Claim Rejections - 35 USC § 101

4. Rejection of claims 2-4 under 35 USC 101, with respect to invention directed to non-statutory subject matter is withdrawn because the claims have been cancelled.

5. Newly added claims 6-18 contains subject matter present in previously rejected claims 2-5. Applicants' arguments filed on 6/11/01 in reference to claims 2-5 have been fully considered but they are not persuasive. Thus, claims 6-18 are rejected under 35 USC 101 for lack of utility, for reasons set forth in Paper No: 19.

Applicants' argue that since the SEQ ID Nos: 31 and 56 are expressed in a human carcinoma cell line, they are useful as diagnostic markers of cancer and to treat or inhibit tumors. Isolation of a nucleotide or protein from a particular cancer cell line does not automatically qualify that protein or nucleotide sequence to be marker for cancer. For example, β-actin can be isolated from most tumor cell lines. However, they are not considered markers for cancer (Fisher et al. U.S. Patent Number 5,710,137). In

addition, there are no controls with non-tumor cell lines to correlate the expression of the above nucleotide sequences (SEQ ID Nos: 31 and 56). Furthermore, Applicants' claims that the nucleotides of the present invention can be used in the production of antibody, tissue markers, chromosome markers and probes. Although these utilities are credible, they are not substantial or specific. For example, the specification does not disclose specific DNA sequences which could be used for the antibody production and for the markers. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 112

6. Claims 6-18 are rejected under U.S.C. 112 first paragraph, for reasons set forth in Paper Number 19. The newly added claims 6-18, contain subject matter present in previously rejected claim 2-5. Applicants' arguments have been fully considered but they are not persuasive for the reasons given above in paragraph 5. Therefore the rejection is maintained.

New Ground of Rejections

The following is a new ground of rejection necessitated by applicants' amendment.

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claims 7 and 10 are rejected as vague and indefinite in the recitation of the phrase "fragment". It is unclear what fragment is encompassed in the instant claims. Therefore, the metes and bounds of the claim are unclear. Claim 11-18 are rejected insofar as it depends on claims 7 and 10.

7b. Claim 9 is rejected as vague and indefinite for reciting "allelic variant", because the term "allelic variant" is not defined in the specification. Therefore, the metes and bounds of the claim is unclear. This is because a variant may encompass a single amino acid change or several amino acid changes and it is unclear what "allelic variants" are encompassed in this claim. Claims 11-18 are rejected insofar as they depend on claim 9.

7c. Claim 11 is rejected as vague and indefinite for reciting the phrase "stringent conditions". Stringency is a relative term, and the art does not recognize a single set of conditions as "stringent". The specification also does not provide an unambiguous definition for the term. In the absence of a recitation of clear hybridization conditions, claim 11 fails to define the metes and bounds of the claim.

Claim Rejections - 35 USC § 112, first paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8a. Claims 7 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses sequences of SEQ ID Nos: 6, 31 and 56. This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose any fragment of the nucleotide sequences 31 and 56 or nucleotide encoding the fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6 or a nucleotide which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6. The claims as written, however, encompass nucleotide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 7, 10 and 11. The specification does not provide written to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of an isolated nucleotide sequence encoding the amino acid of SEQ ID No: 6 and nucleotide sequences of SEQ ID Nos: 31 and 56, the skilled artisan cannot envision all the detailed chemical structure of the claimed nucleotides, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen*

Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only an isolated nucleotide sequence encoding the amino acid of SEQ ID No: 6 and nucleotide sequences of SEQ ID Nos: 31 and 56, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various nucleotide sequences set forth in claims 7,9 and 10. Claims 11-18 are rejected insofar as they depend on claims 7, 9 and 10.

Applicants are reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8b. Claims 8-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleotide encoding SEQ ID NO:6 and nucleotide sequences SEQ ID Nos: 31 and 56, does not reasonably provide enablement for any fragment of the nucleotide sequences 31 and 56 or nucleotide encoding the fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6 or a nucleotide which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims read on any fragment of the nucleotide sequences 31 and 56 or nucleotide encoding the fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6 or a nucleotide which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6. However, other than nucleotide encoding SEQ ID NO:6 and nucleotide sequences SEQ ID Nos: 31 and 56, the specification as filed fails to disclose any other polypeptide sequences.

Despite knowledge in the art for producing nucleotides that are fragments and allelic variants, the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the function of the protein claimed.

Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which fragments and allelic variants would retain the functions of the protein is well outside the realm of routine experimentation. Thus, an undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicants have not taught how one of skill in the art would use the full scope of nucleotide sequences encompassed by the invention of claims 7, 10 and 11. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require an undue amount of trial and error experimentation to determine the functional sequences. Given the breadth of claims 7,10 and 11 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior art of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 11-18 are rejected insofar as they depend on claims 7, 9 and 10.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9a. Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Tomalski et al (U.S. Patent NO: 5,266,317).

The instant invention is directed to an isolated nucleic acid molecule comprising a fragment of the nucleotide sequence set forth in SEQ ID NO: 31 or 56, wherein the fragment comprises at least 10 nucleotides.

Tomalski et al. teaches the gene encoding insect-specific paralytic neurotoxins. The prior art sequence reads on the fragments of the nucleotide sequence set forth in SEQ ID NO: 31 or 56, wherein fragment comprises at least 10 nucleotides. Therefore, the disclosure of Tomalski et al. anticipates claim 7. Claims 11-18 are rejected insofar as they depend on claim 7.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

9b. Claim 10 is rejected under 35 U.S.C. 102(e) as being anticipated by Grotendorst (U.S. Patent NO: 5,770,209).

The instant invention is directed to an isolated nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6, wherein the fragment comprises at least 5 contiguous amino acid residues of the amino acid sequence of SEQ ID NO: 6.

Grotendorst et al. teaches the gene encoding insect-specific paralytic neurotoxins. The prior art sequence reads on the nucleotide sequence encoding the fragments of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6, wherein fragment comprises at least 5 contiguous amino acid. Therefore, the disclosure of Grotendorst et al anticipates claim 10. Claims 11-18 are rejected insofar as they depend on claim 7.

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS
August 23, 2001

JEFFREY STUCKER
PRIMARY EXAMINER